Effects of Reduction in Smoking on Urinary Metabolites of a Tobacco-Specific Lung Carcinogen

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Abstinence from tobacco exposure is the best way to prevent tobacco-related cancer. However, cessation programs have had relatively modest success rates and smoking prevalence rates have not changed markedly in the U.S. in the past ten years. A potential alternative treatment to reduce risk, for those unwilling or unable to quit, is reduction of tobacco use. Limited data are available on the effects of reduction of cigarette consumption on tobacco carcinogen uptake. Because of compensation and other factors, reduction in cigarette consumption may not lead to a concomitant reduction in carcinogen exposure. Benowitz et al (1986) and Hurt et al (2000) previously showed that smoking fewer cigarettes may reduce exposure to toxins, but to a lesser extent than expected. 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) is a potent systemic lung carcinogen in rats and is likely to play a significant role as a cause of lung cancer in smokers. NNK uptake can be estimated by measuring two of its main metabolites: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronides (NNAL-Gluc) in urine. In this study, we investigated the effects of reduced smoking on levels of NNAL and NNAL-Gluc in urine. Urine samples were taken a baseline, and then after 4, 6 and 8 weeks of a smoking reduction program in which smokers used nicotine replacement therapy as an aid to reduction. In 15 subjects who achieved reductions (cigarettes/day) of at least 45% (4 weeks) and 65% (6, 8 weeks), corresponding reductions in NNAL plus NNAL-Gluc were 38.8 ± 64.3, 42.0 ± 52.1, and 27.8 ± 61.5%, respectively. In 6 of 15 subjects, NNAL plus NNAL-Gluc was reduced by > 50% at week 8. In 20 individuals who achieved reductions of at least 45% in cigarettes/day at weeks 4-8, corresponding reductions in NNAL plus NNAL-Gluc were 42.7 ± 64.3 (week 4), 45.8 ± 52.1 (week 6), and 32.6 ± 61.5% (week 8). The results of this study demonstrate that reduction of uptake of the tobacco-specific lung carcinogen NNK can be achieved in some individuals by reduced smoking. The authors thank Ky-anh Le for technical assistance and Susan Schulte for statistical analyses.

PM3003732245

Source: https://www.industrydocuments.ucsf.edu/docs/pxmj0001